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TITLE: Optimized ^{52}Mn Production for Long-lived PET Applications

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ABSTRACT BODY:

Abstract Body: Introduction

^{52}Mn ($t_{1/2}$ =5.59 d, ß$^+$ = 29.6%, Eß$_{max}$ = 0.58 MeV) presents itself as an excellent candidate for a variety of PET applications. Chelation of ^{52}Mn would allow for radiolabelled antibody imaging 2-4 weeks post-injection, and free ^{52}Mn^{2+} has shown promise as a reporter gene probe in stem cell tracking applications [1]. The goals of this work were to develop an efficient ^{52}Mn production target, to optimize separation chemistry, and to demonstrate effective chelation.

Methods

^{52}Mn was produced by 16 MeV proton irradiation of natural chromium metal (approximately 750 mg, 99.999%, GFS chemicals) hydraulically pressed into 0.5 mm thick silver disk. With direct jet water cooling on the rear face, these targets were shown to withstand 60 µA of beam current for one hour without failure. Targets were etched by 2 mL 12.1M HCl and then diluted with 48 mL ethanol and 0.5 mL of 12.1M HCl. ^{52}Mn was radiochemically isolated from the target solution (96% Ethanol, 0.12M HCl) by loading the activity onto approximately 150 mg of AG-1x8 strong anion exchange resin, followed by rinsing. ^{52}Mn was eluted in 1 mL of 6M HCl, before repeating the purification with two additional separation cycles. The final product was eluted in approximately 500 µL of 0.1M HCl. DOTA labeling was performed at pH 4 using 0.25M pH 4.5 NaOAc to buffer the activity.

Results

Average end of bombardment ^{52}Mn yield was 0.14 ± 0.05 mCi/µAh (n=4). Radionuclidic purity was measured to be greater than 99% by high-purity germanium analysis. Target etching resulted in approximately 450 mg of chromium metal dissolution. An average radiochemical separation yield of 72 ± 17% (n=2) has been observed. Total chromium mass in the separated product was measured to be 1.1 ± 0.1 µg (n=1) by microwave plasma atomic emission spectrometry, corresponding to an overall separation factor of approximately 1.6 x 10^5. DOTA chelation of ^{52}Mn was found to be complete after one hour at room temperature, resulting in a measured effective specific activity of 0.05 Ci/µmol (n=1).

Conclusions

Production, separation, and chelation of ^{52}Mn have been demonstrated with very simple targetry and chemistry. These methods significantly improve over previous techniques [2-3] by improving Cr target purity from 99.95% to 99.999% and by allowing for a trap-and-release chromatographic separation. With such an approach, specific activities have been increased and the ^{52}Mn production process can be automated to reduce radiation dose to personnel. These developments will allow for rapid translation into imaging applications.

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References
[1] CM Lewis, SA Graves, *et al.*, Theranostics, 5(3): 227-239, 2015.
[2] S Lahiri, *et al.*, Anal Chem, 78: 7517–21, 2006.
[3] GJ Topping, *et al.*, Med Phys, 40: 042502, 2013.

TABLE TITLE:
Trace Metal Analysis of Mn52 Product

Trace Metal Analysis of Mn52 Product

Element	Mass (µg, ±10%)
Cr	1.07
Mn	0.11
Fe	0.19
Co	0.00
Ni	0.00
Cu	0.14
Zn	3.30

Table 1: Trace metal analysis by microwave plasma atomic emission spectrometry of the radiochemically separated Mn52 product.

(No Image Selected)